CLAIMS

1. A method for screening a test compound for the potential to prevent, stabilize, or treat an autoimmune disease comprising the steps of:

   a) contacting a first blood sample from a first mammal that has, or is at risk for developing, an autoimmune disease with said test compound;

   b) contacting a second blood sample from a second mammal that does not have, or is not predisposed to developing, an autoimmune disease with said test compound, wherein said first and second mammals are of the same species and said first and second blood samples are contacted with said test compound in the same manner; and

   c) measuring leukocyte viability in said first and second samples, wherein said compound is determined to have said potential if said leukocyte viability in said first sample is decreased relative to said leukocyte viability in said second sample.

2. The method of claim 1, wherein said sample of step a) comprises leukocytes that overexpress a receptor for the group consisting of FasL, TNF-alpha, IL-1beta, IL-6, IL-12, and IFN-gamma.

3. The method of claim 1, wherein said sample of step a) comprises leukocytes that are deficient in the expression of CD180.

4. The method of claim 1, wherein said first blood sample comprises autoimmune splenocytes, autoimmune T lymphocytes, autoimmune B lymphocytes, or autoimmune cells of bone marrow origin.

5. The method of claim 1, wherein an apoptotic event is used to measure said viability.

6. A method for screening a test compound for the potential to prevent, stabilize, or treat an autoimmune disease comprising the steps of:

a) partitioning a first blood sample from a first mammal that has, or is at risk for developing, an autoimmune disease into a first fraction which is contacted with an inhibitor of apoptosis and a second fraction which is not contacted with an inhibitor of apoptosis;

b) contacting said first and second fractions with an inhibitor of apoptosis;

c) measuring the ratio of leukocyte viability in said first fraction of step b) to the leukocyte viability in said second fraction of step b);

d) partitioning a second blood sample from a second mammal of the same species as said first mammal, wherein said second mammal does not have, or is not at risk for developing, an autoimmune disease, into a third fraction which is contacted with an inhibitor of apoptosis and a fourth fraction which is not contacted with an inhibitor of apoptosis;

e) contacting said third and fourth fractions with said inhibitor of apoptosis in the same manner that said first and second fractions are contacted with said inhibitor; and

f) measuring the ratio of leukocyte viability in said third fraction of step e) to the leukocyte viability in said fourth fraction of step e),

wherein said compound is determined to have said potential if said ratio of step c) is greater than the ratio of step f).

7. The method of claim 1, wherein a necrotic event is used to measure said cell viability.

8. A method for screening a test compound for the potential to prevent, stabilize, or treat an autoimmune disease comprising the steps of:

a) partitioning a first blood sample from a first mammal that has, or is at risk for developing, an autoimmune disease into a first fraction which is contacted with an inhibitor of necrosis and a second fraction which is not contacted with an inhibitor of necrosis;

b) contacting said first and second fractions with an inhibitor of necrosis;

c) measuring the ratio of leukocyte viability in said first fraction of step b) to the leukocyte viability in said second fraction of step b);

d) partitioning a second blood sample from a second mammal of the same species as said first mammal, wherein said second mammal does not have, or is not at risk for developing, an autoimmune disease into a third fraction which is contacted with an inhibitor of necrosis and a fourth fraction which is not contacted with an inhibitor of necrosis;

e) contacting said third and fourth fractions with said inhibitor of necrosis in the same manner that said first and second fractions are contacted with said inhibitor; and

f) measuring the ratio of leukocyte viability in said third fraction of step e) to the leukocyte viability in said fourth fraction of step e),

wherein said compound is determined to have said potential if said ratio of step c) is greater than the ratio of step f).

9. A method for screening a test compound for the potential to prevent, stabilize, or treat an autoimmune disease comprising the steps of:

a) contacting a population of autoimmune cells from a mammal that has, or is at risk for developing, an autoimmune disease with said test

compound;

b) contacting a second blood element from said mammal with said test compound, wherein said autoimmune cells and said second blood element are contacted with said test compound in the same manner; and

c) measuring the viability of said autoimmune cells, wherein said test compound is determined to have said potential if the viability of said autoimmune cell decreases relative to said second blood element.

10. The method of claim 9, wherein said second blood element is a non-autoimmune leukocyte.

11. The method of claim 9, further comprising the steps of:

i) prior to step a), partitioning said population of autoimmune cells of into a first fraction which is contacted with said compound and a second fraction which is not contacted with said compound; and

ii) after step b), measuring the ratio of viable autoimmune cells of said first fraction to said second blood element and measuring the ratio of said second fraction to said second blood element,

wherein said compound is determined to have said potential if said ratio of said first fraction to said second blood element is less than said ratio of said second fraction to said second blood element.

12. A method for diagnosing an autoimmune disease, or a predisposition to said disease, in a mammal comprising the steps of:

a) obtaining a first blood sample from a first mammal;

b) obtaining a second blood sample from a second mammal of the same species as said first mammal, wherein said second mammal does not

have, or is not at risk for developing, said autoimmune disease;

c) contacting said first blood sample and said second blood sample with a compound that preferentially decreases the viability of leukocytes, wherein both of said first and second samples are contacted with said compound in the same manner; and

d) measuring the viability of leukocytes in said first blood sample and in said second blood sample, wherein a decrease in the leukocyte viability in said first sample relative to the leukocyte viability in said second sample indicates that said first mammal has, or is predisposed to developing, said autoimmune disease.

13. The method of claim 12, wherein said autoimmune disease is Alopecia, Areata, Ankylosing Spondylitis, Antiphospholipid Syndrome, Autoimmune Addison's Disease, Autoimmune Hemolytic Anemia, Autoimmune Hepatitis, Behcet's Disease, Bullous Pemphigoid, Cardiomyopathy, Celiac Sprue-Dermatitis, Chronic Fatigue Immune Dysfunction Syndrome (CFIDS), Chronic Inflammatory Demyelinating Polyneuropathy, Churg-Strauss Syndrome, Cicatricial Pemphigoid, CREST Syndrome, Cold Agglutinin Disease, Crohn's Disease, Discoid Lupus, Essential Mixed Cryoglobulinemia, Fibromyalgia-Fibromyositis, Graves' Disease, Guillain-Barré, Hashimoto's Thyroiditis, Hypothyroidism, Idiopathic Pulmonary Fibrosis, Idiopathic Thrombocytopenia Purpura (ITP), IgA Nephropathy, Insulin dependent Diabetes, Juvenile Arthritis, Lichen Planus, Lupus, Ménière's Disease, Mixed Connective Tissue Disease, Multiple Sclerosis, Myasthenia Gravis, Pemphigus Vulgaris, Pernicious Anemia, Polyarteritis Nodosa, Polychondritis, Polyglandular Syndromes, Polymyalgia Rheumatica, Polymyositis and Dermatomyositis, Primary Agammaglobulinemia, Primary

Biliary Cirrhosis, Psoriasis, Raynaud's Phenomenon, Reiter's Syndrome, Rheumatic Fever, Rheumatoid Arthritis, Sarcoidosis, Scleroderma, Sjögren's Syndrome, Stiffman Syndrome, Takayasu Arteritis, Temporal Arteritis/Giant Cell Arteritis, Ulcerative Colitis, Uveitis, Vasculitis, Vitiligo, Wegener's Granulomatosis, or myasthenia gravis.

14. The method of claim 13, wherein said autoimmune disease is Insulin-dependent Diabetes.

15. The method of claim 12, wherein said leukocytes overexpress a receptor for the group of chemokines consisting of FasL, TNF-alpha, IL-1beta, IL-6, IL-12, and IFN-gamma.

16. The method of claim 12, wherein said leukocytes overexpress B cell maturation protein (BCMA).

17. The method of claim 12, wherein said leukocytes are deficient in the expression of CD180.

18. The method of claim 12, wherein said mammal is a human.

19. The method of claim 12, wherein said compound is TNF-alpha.

20. The method of claim 12, wherein said compound is a TNF-alpha receptor agonist.

21. The method of claim 20, wherein said compound is a humanized or

human monoclonal antibody.

22. The method of claim 12, wherein said compound binds to a Toll-like receptor on a B cell.

23. The method of claim 22, wherein said compound is BCG.

24. The method of claim 22, wherein said cell is deficient in the expression of CD180.

25. A method for diagnosing an autoimmune disease, or a predisposition to said disease, in a mammal comprising the steps of:

a) contacting autoimmune cells from a mammal that has an autoimmune disease, or is at risk for developing an autoimmune disease, with said test compound;

b) contacting a second blood element from said mammal with said test compound, wherein said autoimmune cells and said second blood element are contacted with said compound in the same manner; and

c) measuring the viability of said autoimmune cells, wherein said mammal has, or is at risk for developing, said autoimmune disease if the viability of said autoimmune cells decreases relative to said second blood element.

26. The method of claim 25, wherein said autoimmune disease is Alopecia, Areata, Ankylosing Spondylitis, Antiphospholipid Syndrome, Autoimmune Addison's Disease, Autoimmune Hemolytic Anemia, Autoimmune Hepatitis, Behcet's Disease, Bullous Pemphigoid, Cardiomyopathy, Celiac Sprue-

Dermatitis, Chronic Fatigue Immune Dysfunction Syndrome (CFIDS), Chronic Inflammatory Demyelinating Polyneuropathy, Churg-Strauss Syndrome, Cicatricial Pemphigoid, CREST Syndrome, Cold Agglutinin Disease, Crohn's Disease, Discoid Lupus, Essential Mixed Cryoglobulinemia, Fibromyalgia-Fibromyositis, Graves' Disease, Guillain-Barré, Hashimoto's Thyroiditis, Hypothyroidism, Idiopathic Pulmonary Fibrosis, Idiopathic Thrombocytopenia Purpura (ITP), IgA Nephropathy, Insulin dependent Diabetes, Juvenile Arthritis, Lichen Planus, Lupus, Ménière's Disease, Mixed Connective Tissue Disease, Multiple Sclerosis, Myasthenia Gravis, Pemphigus Vulgaris, Pernicious Anemia, Polyarteritis Nodosa, Polychondritis, Polyglandular Syndromes, Polymyalgia Rheumatica, Polymyositis and Dermatomyositis, Primary Agammaglobulinemia, Primary Biliary Cirrhosis, Psoriasis, Raynaud's Phenomenon, Reiter's Syndrome, Rheumatic Fever, Rheumatoid Arthritis, Sarcoidosis, Scleroderma, Sjögren's Syndrome, Stiffman Syndrome, Takayasu Arteritis, Temporal Arteritis/Giant Cell Arteritis, Ulcerative Colitis, Uveitis, Vasculitis, Vitiligo, Wegener's Granulomatosis, or myasthenia gravis.

27. The method of claim 26, wherein said autoimmune disease is Insulin-dependent Diabetes.

28. The method of claim 25, wherein said second blood element is a non-autoimmune leukocyte.

29. The method of claim 25, further comprising the following steps:

i) prior to step a), obtaining a first blood sample from said mammal and measuring the ratio of viable autoimmune cells to said second blood

element in said first blood sample;

ii) during step a), administering said compound to said mammal;

iii) after step a), obtaining a second blood sample from said mammal and measuring the ratio of viable autoimmune cells to said second blood element in said second blood sample,

wherein said mammal has, or is predisposed to having, said autoimmune disease if the ratio of step iii) is less than the ratio of step i).

30. The method of claim 25, wherein said mammal is a human.

31. The method of claim 25, wherein said compound is TNF-alpha.

32. The method of claim 25, wherein said compound is a TNF-alpha receptor agonist.

33. The method of claim 32, wherein said compound is a humanized or human monoclonal antibody.

34. The method of claim 25, wherein said compound binds to a Toll-like receptor on a B cell.

35. The method of claim 34, wherein said compound is BCG.

36. The method of claim 34, wherein said cell is deficient in the expression of CD180.

37. A method for the stratification of a human patient into a therapeutic

subgroup for an autoimmune disease comprising the steps of:

a) contacting a blood sample from said patient with a compound that preferentially decreases the viability of leukocytes;

b) measuring the viability of said leukocytes; and

c) placing said patient into a therapeutic subgroup based on the amount of decrease of said viability.

38. The method of claim 37, wherein said leukocytes overexpress a receptor for the group of chemokines consisting of FasL, TNF-alpha, IL-1beta, IL-6, IL-12, and IFN-gamma.

39. The method of claim 37, wherein said leukocytes overexpress B cell maturation protein (BCMA).

40. The method of claim 37, wherein said leukocytes are deficient in the expression of CD180.

41. The method of claim 37, wherein said viability is measured relative to the cell viability of leukocytes in a second blood sample obtained from a human that does not have, or is not predisposed to having, said autoimmune disease, wherein said second blood sample and said blood sample of step (a) are contacted with said compound in the same manner and said patient is placed into said subgroup based on the relative decrease of said viability.

42. The method of claim 37, wherein said viability is a measure of leukocyte viability in said sample relative to a second blood element in said sample, wherein said second blood element and said blood sample of step (a) are

contacted with said compound in the same manner and said patient placed into said subgroup based on the relative decrease of said viability.

43. The method of claim 42, wherein said second blood element is a non-autoimmune leukocyte.

44. The method of claim 42, wherein said compound is administered to said patient.

45. The method of claim 42, further comprising the following steps:

i) prior to step a), obtaining a first blood sample from said mammal and measuring the ratio of viable autoimmune cells to said second blood element in said first blood sample;

ii) during step a), administering said compound to said mammal;

iii) after step a), obtaining a second blood sample from said mammal and measuring the ratio of viable autoimmune cells to said second blood element in said second blood sample,

wherein the decrease in the ratio of step iii) to the ratio of step i) determines the severity or course of said disease.

46. The method of claim 37, wherein said autoimmune disease is Alopecia, Areata, Ankylosing Spondylitis, Antiphospholipid Syndrome, Autoimmune Addison's Disease, Autoimmune Hemolytic Anemia, Autoimmune Hepatitis, Behcet's Disease, Bullous Pemphigoid, Cardiomyopathy, Celiac Sprue-Dermatitis, Chronic Fatigue Immune Dysfunction Syndrome (CFIDS), Chronic Inflammatory Demyelinating Polyneuropathy, Churg-Strauss Syndrome, Cicatricial Pemphigoid, CREST Syndrome, Cold Agglutinin

Disease, Crohn's Disease, Discoid Lupus, Essential Mixed Cryoglobulinemia, Fibromyalgia-Fibromyositis, Graves' Disease, Guillain-Barré, Hashimoto's Thyroiditis, Hypothyroidism, Idiopathic Pulmonary Fibrosis, Idiopathic Thrombocytopenia Purpura (ITP), IgA Nephropathy, Insulin dependent Diabetes, Juvenile Arthritis, Lichen Planus, Lupus, Ménière's Disease, Mixed Connective Tissue Disease, Multiple Sclerosis, Myasthenia Gravis, Pemphigus Vulgaris, Pernicious Anemia, Polyarteritis Nodosa, Polychondritis, Polyglandular Syndromes, Polymyalgia Rheumatica, Polymyositis and Dermatomyositis, Primary Agammaglobulinemia, Primary Biliary Cirrhosis, Psoriasis, Raynaud's Phenomenon, Reiter's Syndrome, Rheumatic Fever, Rheumatoid Arthritis, Sarcoidosis, Scleroderma, Sjögren's Syndrome, Stiffman Syndrome, Takayasu Arteritis, Temporal Arteritis/Giant Cell Arteritis, Ulcerative Colitis, Uveitis, Vasculitis, Vitiligo, Wegener's Granulomatosis, or myasthenia gravis.

47. The method of claim 46, wherein said autoimmune disease is Insulin-dependent Diabetes..

48. A method for monitoring a therapy for a human that has an autoimmune disease, or is at risk for developing said disease, comprising the steps of:

i) obtaining a first blood sample from said patient and contacting said first blood sample with a compound that preferentially decreases the viability of leukocytes;

ii) measuring the viability of leukocytes in said first blood sample;

iii) obtaining a second blood sample from said patient and contacting said second blood sample with said compound, wherein said second blood sample is obtained at least 12 hours after obtaining said first blood

sample;

iv) measuring the viability of leukocytes in said second blood sample; and

v) determining the efficacy of said therapy based on leukocyte viability, wherein an increase in said viability indicates that said therapy is efficacious.

49. The method of claim 48, wherein said viability is measured relative to the cell viability of leukocytes in a second blood sample obtained from a human not having or not predisposed to said autoimmune disease, wherein said second blood sample and said blood sample of step (a) are contacted with said compound in the same manner.

50. The method of claim 48, wherein said viability is a measure of autoimmune cell viability in said sample relative to a second blood element in said sample.

51. The method of claim 50, wherein said second blood element is a non-autoimmune leukocyte.

52. The method of claim 50, wherein said second blood element is an erythrocyte.

53. The method of claim 48, wherein said compound is administered to said patient.

54. The method of claim 48, wherein said autoimmune disease is Alopecia,

Areata, Ankylosing Spondylitis, Antiphospholipid Syndrome, Autoimmune Addison's Disease, Autoimmune Hemolytic Anemia, Autoimmune Hepatitis, Behcet's Disease, Bullous Pemphigoid, Cardiomyopathy, Celiac Sprue-Dermatitis, Chronic Fatigue Immune Dysfunction Syndrome (CFIDS), Chronic Inflammatory Demyelinating Polyneuropathy, Churg-Strauss Syndrome, Cicatricial Pemphigoid, CREST Syndrome, Cold Agglutinin Disease, Crohn's Disease, Discoid Lupus, Essential Mixed Cryoglobulinemia, Fibromyalgia-Fibromyositis, Graves' Disease, Guillain-Barré, Hashimoto's Thyroiditis, Hypothyroidism, Idiopathic Pulmonary Fibrosis, Idiopathic Thrombocytopenia Purpura (ITP), IgA Nephropathy, Insulin dependent Diabetes, Juvenile Arthritis, Lichen Planus, Lupus, Ménière's Disease, Mixed Connective Tissue Disease, Multiple Sclerosis, Myasthenia Gravis, Pemphigus Vulgaris, Pernicious Anemia, Polyarteritis Nodosa, Polychondritis, Polyglandular Syndromes, Polymyalgia Rheumatica, Polymyositis and Dermatomyositis, Primary Agammaglobulinemia, Primary Biliary Cirrhosis, Psoriasis, Raynaud's Phenomenon, Reiter's Syndrome, Rheumatic Fever, Rheumatoid Arthritis, Sarcoidosis, Scleroderma, Sjögren's Syndrome, Stiffman Syndrome, Takayasu Arteritis, Temporal Arteritis/Giant Cell Arteritis, Ulcerative Colitis, Uveitis, Vasculitis, Vitiligo, Wegener's Granulomatosis, or myasthenia gravis.

55. The method of claim 54, wherein said autoimmune disease is Insulin-dependent Diabetes.